Strength vs Aerobic Training in Children With Cystic Fibrosis*

A Randomized Controlled Trial

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Study objective: **Exercise has the potential to improve the ability of a patient with cystic fibrosis (CF) to cope with the physical demands of everyday life, and may improve prognosis. The purpose of this study was to compare the effects of a home-based, semi-supervised, upper-body strength-training regimen with a similarly structured aerobic training regimen.**

Design: **Data were collected during a 1-year randomized clinical trial.**

Setting: **Counselors conducted in-home visits with the participants once per week for the first 8 weeks followed by monthly visits for the remainder of the study.**

Patients: **Sixty-seven patients with CF, aged 8 to 18 years, participated in the trial.**

Intervention: **Participants in both exercise conditions were encouraged to exercise at least three times per week for 1 year. Each child in the aerobic group was given a stair-stepping machine, and each child in the upper-body strength training group was given an upper-body-only weight-resistance machine.**

Measures and results: **Aerobic fitness, pulmonary function, quality of life, and strength were measured at baseline, at 6 months, and at 12 months. Strength training increased the maximum weight lifted for biceps curls significantly more than aerobic training ($p < 0.02$). However, this differential did not remain significant after control for increase in height. Both training procedures were associated with increased strength ($p < 0.002$) and physical work capacity (PWC) [$p < 0.033$].**

Conclusions: **We concluded that strength and aerobic training may increase upper-body strength, and that both types of training may increase PWC for children with CF. Future trials should be conducted with no-training control subjects and larger samples to increase statistical power.**

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Key words: aerobic fitness; cystic fibrosis; exercise; muscle strength

Abbreviations: CF = cystic fibrosis; GEE = generalized estimating equation; IRB = Institutional Review Board; PWC = physical work capacity; QWB = quality of well-being; $\dot{V}o_2$peak = maximum oxygen consumption

Cystic fibrosis (CF) is the most common profoundly life-shortening inherited disorder among white populations, affecting 1 in 3,300 live white births.[1] Despite discovery of the CF gene in 1989, no curative treatment has yet been developed. A defect in chloride ion transport across epithelial surfaces results in the accumulation of viscid mucus, endobronchial infection, and inflammation leading to progressive lung damage, and premature mortality.[2–4] With advances in infection control, life expectancy has been extended from a median survival of 20 years in 1981,[5] to a median of 31.3 years as of 1998.[6] Aerobic fitness has been associated with improved prognosis.[7,8] Less-fit patients with CF were three times less likely to survive 8 years than those who achieved aerobic fitness.[7] Conversely, the detraining effects of a sedentary lifestyle contribute to functional deterioration in individuals with CF.[9]

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Studies[10–15] have suggested that individuals with CF are less fit than peers. However, physical activity training has increased exercise tolerance in children with CF.[12,16] Exercise has increased work capacity, improved cardiorespiratory fitness, improved ventilatory muscle endurance, and enhanced immune function, and resulted in a training bradycardia, although considerable individual variation has been noted.[7,11,14,17–19] While increased exercise may not improve pulmonary function, the slowing of progressive pulmonary decline could be an important benefit.[20] No study of individuals with CF has demonstrated harm from exercise. The occasional patient who experiences exercise-related oxygen desaturation can maintain adequate oxygenation through the use of supplemental oxygen during exercise.[21–23]

Exercise might acutely enhance pulmonary function due to its ability to mobilize airway mucus.[24–26] In a meta-analysis,[27] adding exercise to standard chest physiotherapy resulted in a clinically important and statistically significant improvement in FEV_1. Although there are insufficient data to draw definitive conclusions about the relative efficacy of exercise vs chest physical therapy, exercise is often recommended as an alternative, for which compliance may be easier.[28–31]

Several studies[11–14,16–18,24,25,32–37] of CF exercise programs showed results dependent on compliance and intensity of training. The best results have been achieved with supervised programs.[11,12,17,18,24,34] For example, we conducted a 3-month group-jogging program[11] that resulted in increased exercise tolerance and cardiopulmonary fitness in exercising patients compared with nonexercising control patients. Other programs with swimming, trampoline jumping, and cycling have also shown positive effects on exercise tolerance[17] work capacity or physical fitness,[16,37,38] leg strength, sputum production,[14,24] dyspnea,[13] and pulmonary function.[24,25] Few studies have lasted long enough to examine the long-term effects of an exercise program on pulmonary function, life function, or prognosis. It is known that 8-year survival is significantly correlated with baseline fitness,[7] suggesting a possible role for exercise in prolonging the lives of patients with CF. A recent retrospective analysis by Nixon et al[39] indicated that the amount of time spent engaging in vigorous physical activity was significantly less for children with CF as compared to healthy children and, correspondingly, the patients with CF had significantly lower maximum oxygen consumption ($\dot{V}O_2$peak) values as compared to the healthy children.[39] These results suggest a need for more intensive interventions.

Since many patients live at long distance from their CF centers, home-based programs may be the most feasible. However, studies of home-based, but minimally supervised interventions have been limited, with mixed results. Holzer et al[32] reported significant compliance problems and no notable improvement in fitness. de Jong et al[40] described a home-based, semisupervised exercise program for CF youth using bicycle ergometers and a biweekly home visit from an investigator that evidenced increased maximal work capacity, maximal oxygen uptake, and anaerobic threshold at the end of the 3-month training program. More recently, Gulmans et al[38] tested a 6-month in-home training program. Young patients with CF were asked to ride a stationary bicycle for 16 min five times per week at an intensity level equal to 70 to 80% of their maximal heart rate. A physiotherapist supervised one session per week. The intervention resulted in a significant increase in maximum ventilatory oxygen capacity. This suggests that adherence to an exercise protocol and improved fitness can be achieved when supervised at home.

The benefits of strength training for patients with CF also have not been fully evaluated. The only published study of weight training suggested a number of benefits, including an increase in muscle strength, muscle size, and body weight, and a reduction in residual lung volume, which was attributed to increased elasticity and mobility of the chest wall.[41] Strength training warrants additional investigation both in contrast to and in conjunction with aerobic training.

Conclusions regarding the benefits of an exercise program are hampered by methodologic limitations. Most are uncontrolled studies with small sample sizes, most lack important outcome measures, most focus on short-term interventions with limited follow-up, and many lacked random assignment or a control group. Thus, controlled trials remain necessary in this field.

The purpose of this study was to compare the effects of a home-based, upper-body strength training regimen with an aerobic training regimen over a 1-year period. This study is the first randomized trial with comprehensive outcome measures (fitness, pulmonary function, quality of life) that tested a home-based exercise program for young patients with CF.

Materials and Methods

Experimental Design

A randomized design, with intent-to-treat analysis, was employed. Eligible youth from the Cystic Fibrosis Center at the Children's Hospital of Pittsburgh were assigned at random to either the aerobic or upper-body strength training conditions following baseline strength, aerobic fitness, and pulmonary function measures. Random assignment was determined by the research coordinator from a predetermined list of random numbers. Staff members were notified of each child's assignment immediately following baseline measures, precluding advanced knowledge of assignment, and all measurement staff members remained blind to assignment through follow-up measures. Separate counseling staff remained blind to outcome measures throughout the trial. Investigators remained blind to outcome measures until all youth had completed their 12-month assessment measures. Data were collected in the Cystic Fibrosis Center and transferred to coauthors in San Diego for analysis, thereby ensuring greater separation of clinical and analysis components of the trial. Usual-care control procedures were not included in this trial because the university Institutional Review Board (IRB) suggested this would not be ethical, and because we expected specific directional responses to each intervention.

CF Sample

A total of 143 patients between 8 years and 18 years of age, all of whom had received a diagnosis of CF as a result of a positive sweat test result (sweat chloride and/or sodium concentration > 60 mEq/L after sweat stimulation by pilocarpine iontophoresis) were invited to participate. Participants were excluded if they were already engaging in regular aerobic exercise or weight training for 20 min at least three times per week; their peak work capacity was > 110% of predicted based on the Godfrey equation[42]; their oxygen uptake (millimeters per minute) was > 100% of predicted,[43] based on the Franklin or Rowland equation; their $\dot{V}O_2$peak was > 45 mL/kg/min; or they gave a submaximal effort, which was defined as a respiratory exchange ratio of < 1.0 or a subjective interpretation by the tester, on more than one baseline testing date. Sixty-seven youth qualified and agreed to participate.

Intervention Procedures

Exercise Counseling: Exercise physiology counselors with BA or MA degrees counseled CF youth during home visits on a weekly basis for 8 weeks. They then visited the participants approximately once per month for the remainder of the year. Counselors prompted and praised exercise adherence, instructed safe exercise technique and heart rate monitoring, and gradually increased the exercise prescription.

Exercise Equipment and Prescriptions: Participants were asked to exercise at least three times per week for 12 consecutive months. Children in the aerobic training group were given a stair-stepping machine (Tunturi Variable Resistance Club-style Climber; Tunturi; Redmond, WA), and instructed to exercise 5 min per session, gradually increasing their exercise to 30 min per session over the course of the study. Children were taught to keep gradually increase their target heart rate to 70% of their maximum heart rate.

Participants in the upper-body strength group were given a Nordic Power weight resistance machine (Nordic Track; Chaska, MN) to perform lifting exercises. They were instructed to perform biceps curls, lateral pull-downs, and military and bench presses. These exercises were individually tailored to the participants' strength, and the exercises increased gradually by the number of sets and repetitions as well as by the amount of resistance per bout over the year. Children were instructed to keep their heart rate < 55% of their maximum, based on the baseline exercise test. Attachments for and leg exercise were not recommended in order to decrease the likelihood of lower-body exercise and increase difference in training between groups.

Adherence to Exercise Prescriptions: To assess adherence, participants were given portable heart rate monitors (Polar Vantage XL Heart Monitor, Model 61214; Country Technology; Gays Mills, WI). Counselors taught patients to record the start and stop time of each exercise session, and were instructed to move to 70% in the aerobic group or remain at or < 55% of baseline for the strength group. Participants received financial incentives for participation.

Measures

Measures were obtained at baseline, 6 months, and 12 months at least 2 weeks following high doses of tobramycin, ciprofloxacin, or IV treatments. All tests were completed in the Exercise and the Pulmonary Function Testing Laboratories at the Children's Hospital of Pittsburgh. Prior to testing, the children changed into shorts and t-shirts. The room temperature was kept at 21°C. Resting measures were obtained for 2 min prior to aerobic fitness testing.

Aerobic Fitness Testing: Progressive exercise testing was conducted on an electronically braked cycle ergometer following the Godfrey protocol.[42] Patients began pedaling at 0 W for 1 min, with the workload increasing by 10 W, 15 W, or 20 W each minute depending on the patients' height and clinical status. Maximal effort was encouraged. The peak work capacity was defined as the highest workload (watts) sustained for 1 min, and peak work capacity percentage of predicted was determined from the equations of Godfrey[42] based on height and gender.

Metabolic equipment (Medical Graphics; St. Paul, MN) provided online, breath-by-breath measures of oxygen uptake, carbon dioxide production, minute ventilation, respiratory rate, tidal volume, and end-tidal carbon dioxide tension. Values were printed every 15 s, and peak values were determined from the last 15 s of exercise. A 12-lead ECG was monitored continuously, and heart rate was determined each minute and at peak exercise. Oxyhemoglobin saturation was monitored continuously using a pulse oximeter (Nellcor N-100; Mallinckrodt; Pleasanton, CA) and finger probe, and stable values were recorded during the last 20 s of each minute.

Pulmonary Function Testing: Prior to exercise testing, participants performed pulmonary function tests according to the American Thoracic Society standards. Lung volumes were determined by body plethysmography. Spirometry, including flow-volume curves both before and after inhalation of a bronchodilator (albuterol), was performed using a body plethysmograph (Sensor Medics System 6200; SensorMedics; Yorba Linda, CA), with the patient seated comfortably. The best flow-volume loop, FVC, FEV_1, peak expiratory flow rate, maximal midexpiratory flow rate, and the flow rates at 50% and 25% of vital capacity were chosen from among no fewer than three nor more than eight maneuvers. The "best test" was chosen on the basis of the largest sum of FVC and FEV_1.

Strength Testing: Participants performed a one-repetition maximal lift (*ie*, the maximum amount lifted one time) for bench presses, biceps curls, and leg extensions. For the bench press, participants began by lifting a weight equal to 30% of their body weight, and progressed by 2.5%, 5%, or 10% of body weight, depending on comfort. The biceps curl exercise began at 30% of bench press maximum, and progressed by 2.5%, 5%, or 10% of body weight, depending on comfort. Leg extensions began at 50% of body weight, and progressed by 5%, 10%, or 15% of body weight, depending on comfort.

Quality of Life: Quality of well-being was measured using the quality of well-being QWB scale.[44–46] The dimensions of functioning assessed included mobility, physical activity, and social activity. Questions were asked by a trained interviewer. The system is based on the assignment of a societal "preference weight" to each step of the function scale and to each symptom.

Scores range from 0 (death) to 1 (optimum functioning). If the child was < 12 years old, the interview was conducted with the parent.

Anthropometric Measures: Height and weight were measured with the children in their stocking feet using a stadiometer and a balance beam scale, respectively.

Analysis

Descriptive analyses and *t* tests were computed using SPSS for Windows 6.1.3 (SPSS; Chicago, IL). The distributions were examined and adjusted using natural log transformations or squaring to improve normality. Longitudinal analyses were conducted using the generalized estimating equation (GEE) approach (SAS version 6.12; SAS Institute; Cary, NC). This is well suited for small sample analyses and for correlated data.[47,48] Regression coefficients are estimated by an iterative process that treats the correlation among observations for the same unit of analysis as a nuisance. Specifications of a link function include both continuous and binary dependent variables. *A priori* hypothesis tests employed α levels of < 0.05 and at < 0.1 for bidirectional and unidirectional hypotheses, respectively.

Results

The trial was conducted with 67 youth (2 African Americans and 65 whites). When two siblings were eligible, both were randomly assigned to the same condition. However, only one member of each pair was chosen at random to be included in analyses. There were five sets of siblings. Thus, analyses were conducted for 62 independent youth. The average age at baseline was 11.5 years. Forty-five percent were male, and 32 youth and 30 youth were assigned to the aerobic group and strength group, respectively. There were no significant differences at baseline between the groups with respect to dependent variables, age, or gender, and this balance remained true after loss to follow-up. Seven patients in the aerobic group ($n = 25$) and two patients in the strength group ($n = 28$) were not available for follow-up. Patients missing both posttest and follow-up data were not included in analyses. We did not impute missing data in order to avoid artificial reduction in error variance and consequential increase in type I error, making all statistical analyses conservative.

Several variables required transformation. The natural log transformation was used for physical work capacity, maximum weight bench-pressed, maximum weight used to perform biceps curls, and maximum weight used to perform leg extensions. The percentage of predicted physical work capacity (PWC), and maximum weight used to perform biceps curls/subject's weight were squared to normalize distributions. A definition of each dependent variable is found in Table 1.

Table 1—*Definition of the Dependent Variables*

Dependent Variable Names	Variable Definitions
PWCL	PWC (watts)
PWCPCS	Percentage of predicted PWC
$\dot{V}O_2$PKG	Peak oxygen consumption (milliliters/minute/kilogram)
FEV_1PT	Percentage of predicted FEV_1
BPMAXL	Maximum weight used in bench press (pounds)
BCMAXL	Maximum weight used in biceps curls (pounds)
LEMAXL	Maximum weight used in leg extension (pounds)
BPMXKG	Maximum weight used in bench press (pounds)/subject's weight (kilogram)
LEMXKG	Maximum weight used in leg extension (pounds)/subject's weight (kilogram)
BCMXKS	Maximum weight used in biceps curls (pounds)/subject's weight (kilogram)
TOTSC	Total score from the QWB scale

Bivariate Correlations

Bivariate correlations were calculated between each dependent variable and each of the independent variables (age, sex) at each assessment point. There were two exceptions; FEV_1 percentage of predicted was not correlated with age or gender, and PWC percentage of predicted was not correlated with gender, since these variables are part of the predictive equations. The results show that at baseline, all of the dependent variables except for QWB total score, $\dot{V}O_2$peak, maximum weight used for biceps curls/subject's weight, and maximum weight bench pressed/subject's weight were significantly correlated with age. $\dot{V}O_2$ peak, maximum weight used for biceps curls/subject's weight, and maximum weight bench pressed/subject's weight were significantly greater for male than female subjects. The correlations between age and the dependent variables at 6 months showed the same results as those at baseline. The correlation between gender and maximum weight used for biceps curls/subject's weight did not remain significant at 6 months. The correlations between the dependent variables and the independent variables at 12 months were consistent with those seen at baseline (Table 2). Due to these associations, outcome analyses were adjusted for these covariates, exclusive of baseline values.

Strength Measures

The *a priori* hypotheses were that strength would increase more than seen in the aerobic-training group, and that strength would increase over time within the strength-training group. All strength measures showed a significant increase over time (Table 3). Using the GEE, maximum weight lifted for biceps curls was the only dependent variable that

Table 2—*Correlations of the Dependent Variables With Each of the Independent Variables**

Dependent Variables Time (N size)	Independent Variables: Time 1, Age, r	Time 1, Age, p Value	Time 1, Sex, r	Time 1, Sex, p Value	Time 2, Age, r	Time 2, Age, p Value	Time 3, Age, r	Time 3, Age, p Value
PWCL, W								
1 (62)	0.679	< 0.001	− 0.052	0.689	0.657	< 0.001	0.686	< 0.001
2 (56)	0.649	< 0.001	− 0.147	0.280	0.612	< 0.001	0.642	< 0.001
3 (53)	0.551	< 0.001	− 0.082	0.559	0.508	< 0.001	0.569	< 0.001
PWCPCS								
1 (62)	− 0.302	0.017	0.136	0.291	− 0.239	0.076	− 0.222	0.111
2 (56)	− 0.127	0.352	0.043	0.753	− 0.157	0.247	− 0.178	0.203
3 (53)	− 0.270	0.051	0.119	0.398	− 0.308	0.025	− 0.248	0.074
TOTSC								
1 (62)	− 0.017	0.177	0.094	0.469	− 0.079	0.563	− 0.110	0.432
2 (56)	− 0.184	0.175	0.120	0.377	− 0.202	0.135	− 0.177	0.204
3 (53)	0.095	0.501	0.001	0.944	0.073	0.602	0.093	0.507
$\dot{V}O_2$PKG, mL/min/kg								
1 (62)	− 0.093	0.417	− 0.355	0.005	− 0.049	0.722	− 0.066	0.639
2 (55)	− 0.106	0.443	− 0.489	< 0.001	− 0.151	0.272	− 0.120	0.396
3 (53)	− 0.265	0.055	− 0.481	< 0.001	− 0.306	0.026	− 0.246	0.075
FEV_1PT								
1 (62)	− 0.270	0.034	0.041	0.754	− 0.262	0.051	− 0.312	0.023
2 (56)	− 0.240	0.075	− 0.038	0.782	− 0.232	0.086	− 0.313	0.023
3 (53)	− 0.331	0.015	− 0.113	0.420	− 0.354	0.009	− 0.318	0.020
BCMAXL, lb								
1 (62)	0.731	< 0.001	0.131	0.310	0.706	< 0.001	0.743	< 0.001
2 (56)	0.695	< 0.001	− 0.052	0.705	0.666	< 0.001	0.729	< 0.001
3 (52)	0.691	< 0.001	− 0.113	0.421	0.661	< 0.001	0.702	< 0.001
BCMXKS, lb/kg								
1 (62)	0.094	0.470	− 0.339	0.007	0.043	0.755	0.000	> 0.999
2 (56)	− 0.021	0.881	− 0.250	0.063	− 0.046	0.738	− 0.025	0.860
3 (52)	− 0.009	0.949	− 0.356	0.010	− 0.029	0.839	− 0.007	0.959
BPMAXL, lb								
1 (61)	0.643	< 0.001	− 0.152	0.242	0.582	< 0.001	0.645	< 0.001
2 (56)	0.641	< 0.001	− 0.168	0.217	0.613	< 0.001	0.650	< 0.001
3 (53)	0.532	< 0.001	− 0.201	0.149	0.504	< 0.001	0.548	< 0.001
BPMXKG, lb/kg								
1 (61)	− 0.076	0.560	− 0.340	0.007	− 0.154	0.256	− 0.126	0.368
2 (56)	− 0.157	0.248	− 0.352	0.008	− 0.173	0.202	− 0.124	0.376
3 (53)	− 0.233	0.093	− 0.416	0.002	− 0.254	0.066	− 0.223	0.109
LEMAXL, lb								
1 (62)	0.775	< 0.001	− 0.006	0.965	0.72	< 0.001	0.776	< 0.001
2 (56)	0.783	< 0.001	0.032	0.815	0.761	< 0.001	0.805	< 0.001
3 (53)	0.709	< 0.001	0.084	0.548	0.685	< 0.001	0.726	< 0.001
LEMXKG, lb/kg								
1 (62)	0.463	< 0.001	− 0.061	0.639	0.388	0.003	0.419	0.002
2 (56)	0.410	0.002	− 0.027	0.842	0.391	0.003	0.439	0.001
3 (53)	0.238	0.086	0.011	0.937	0.220	0.113	0.256	0.064

*Numbers represent the effects of each variable in the row for a model and the associated p value. See Table 1 for definition of abbreviations.

showed a significant group-by-time interaction ($p < 0.04$) [Table 3]. However, this difference did not remain significant after control for increase in height.

Maximum Weight Used for Biceps Curls: Maximum weight used for biceps curls showed a steady increase over time in both the aerobic and strength groups. Within-group, paired *t* tests showed a significant increase during the first 6 months for the aerobic group. The significant increase over baseline was maintained at 12 months. The results of the paired *t* tests for the strength group showed that a significant increase occurred in the first 6 months ($p = 0.001$), from 6 months to 12 months, and between baseline and 12 months. The significant change over time produced by the GEE (Table 3) is confirmed by the significant difference seen in the

Table 3—*Statistical Significance (α) by Selected Variables**

Dependent Variables Effects†	Without Covariate‡	Age§¶	Gender‖¶
PWCL, W			
Group	0.588	0.646	0.610
Time	0.025	0.023	0.025
Group × time	0.761	0.622	0.767
PWCPCS			
Group	0.851	NA	NA
Time	0.437	NA	NA
Group × time	0.459	NA	NA
TOTSC			
Group	0.975	0.922	0.968
Time	0.446	0.287	0.447
Group × time	0.164	0.151	0.171
Vo_2PKG, mL/min/kg			
Group	0.584	0.546	0.650
Time	0.039	0.038	0.038
Group × time	0.497	0.533	0.511
FEV_1PT			
Group	0.763	0.680	0.771
Time	0.791	0.778	0.791
Group × time	0.905	0.813	0.899
BCMAXL, lb			
Group	0.745	0.907	0.770
Time	< 0.001	< 0.001	< 0.001
Group × time	0.017	0.034	0.016
BCMXKS, lb/kg			
Group	0.679	0.692	0.728
Time	0.001	0.001	0.001
Group × time	0.113	0.114	0.099
BPMAXL, lb			
Group	0.691	0.496	0.677
Time	< 0.001	< 0.001	< 0.001
Group × time	0.084	0.127	0.075
BPMXKG, lb/kg			
Group	0.573	0.593	0.543
Time	0.024	0.025	0.023
Group × time	0.325	0.311	0.280
LEMAXL, lb			
Group	0.453	0.411	0.453
Time	< 0.001	< 0.001	< 0.001
Group × time	0.230	0.337	0.232
LEMXKG, lb/kg			
Group	0.364	0.379	0.370
Time	< 0.001	< 0.001	< 0.001
Group × time	0.811	0.901	0.805

*See Table 1 for definition of abbreviations. NA = Not applicable.
†Numbers indicate association for the respective effects.
‡First column is reported without a covariate.
§Second column indicates the effects of controlling for age.
‖Third column indicates the effects of controlling for gender.
¶Age and gender were used as covariates in separate GEE analyses.

comparison of baseline to 12 months for both groups (Tables 4, 5).

Maximum Weight Used for Biceps Curls/Subject's Weight: The maximum weight lifted for biceps curls/subject's weight showed an increase over time in both groups. The paired t tests involving maximum weight used for biceps curls/subject's weight showed no significant difference for any of the comparisons across time for the aerobic group. However, the strength group showed a significant increase from 6 months to 12 months and from baseline to 12 months (Table 5).

Maximum Weight Bench Pressed: Maximum weight pressed showed a large increase in the first 6 months for both groups. From 6 months to 12 months, the amount of weight bench pressed in the strength group increased slightly while it remained the same in the aerobic group. The results of the paired t test for the strength group showed significant changes during the first 6 months, as well as from 6 months to 12 months, resulting in a significant increase from baseline to 12 months. The aerobic group had a significant change in the first 6 months that was sustained, to create a significant difference between baseline and 12 months. Changes in strength over time in the aerobic group were not maintained when adjusted for body weight (Tables 4, 5).

Maximum Weight Used for Leg Extensions: Maximum weight used for leg extensions increased over time for both groups. In the strength group, the greatest change occurred in the first 6 months, with a smaller gain occurring from 6 months to 12 months, while the aerobic group showed an approximately linear change over time. The results of the paired t test confirm that both groups showed a significant difference for all three comparisons (Tables 4, 5).

Maximum Weight Used for Leg Extensions/Subject's Weight: Both groups experienced a slight linear increase over time in maximum weight used for leg extensions. The aerobic group showed a significant increase from baseline to 6 months and to 12 months. The strength group showed a significant increase during the first 6 months, and a significant increase from baseline to 12 months. Changes in the amount of weight lifted by leg extensions remained significant after adjustment for body weight in both groups (Tables 4, 5).

Covariate Adjustments: The GEE was repeated twice for each dependent variable, once with age and once with gender as a covariate. Maximum weight used for biceps curls continued to show a significant group-by-time interaction after controlling for age ($p = 0.034$) and sex (0.016). The time effects remained significant for all of the strength-related dependent variables after adjusting for covariates (Table 3).

Table 4—*Comparison of Within-Condition Means Across Time for the Aerobic Group**

Variables	Time 1 vs Time 2 (n = 26)			Time 1 vs Time 3 (n = 25)			Time 2 vs Time 3 (n = 25)		
PWCL, W	4.59 (0.30)	4.66 (0.29)	p = 0.054	4.59 (0.32)	4.68 (0.32)	p = 0.003	4.65 (0.30)	4.68 (0.32)	p = 0.241
PWCPCS	9,181.96 (3,007.3)	9,564.81 (4,554.5)	p = 0.491	9,218.0 (3,063.6)	9,047.32 (3,929.2)	p = 0.666	9,523.04 (4,643.3)	9,047.32 (3,929.2)	p = 0.240
TOTSC	4.99 (0.48)	4.78 (0.61)	p = 0.183	4.97 (0.49)	4.80 (0.63)	p = 0.270	4.79 (0.62)	4.80 (0.63)	p = 0.930
$\dot{V}O_2$PKG, mL/min/kg	34.81 (5.45)	32.90 (6.06)	p = 0.094	34.60 (5.46)	33.69 (7.16)	p = 0.329	33.11 (6.09)	33.69 (7.16)	p = 0.560
FEV_1PT	92.22 (18.33)	89.65 (19.32)	p = 0.191	91.51 (18.34)	90.32 (17.92)	p = 0.558	88.56 (18.88)	90.32 (17.92)	p = 0.363
BCMAXL, lb	3.34 (0.30)	3.42 (0.28)	p = 0.007	3.33 (0.30)	3.46 (0.27)	p = 0.001	3.43 (0.28)	3.46 (0.27)	p = 0.362
BCMXKS, lb/kg	0.670 (0.24)	0.693 (0.21)	p = 0.489	0.680 (0.24)	0.726 (0.31)	p = 0.412	0.712 (0.19)	0.726 (0.31)	p = 0.808
BPMAXL, lb	3.98 (0.31)	4.09 (0.26)	p = 0.004	3.98 (0.32)	4.10 (0.26)	p < 0.001	4.09 (0.27)	4.10 (0.26)	p = 0.685
BPMXKG, lb/kg	1.54 (0.32)	1.62 (0.31)	p = 0.123	1.55 (0.31)	1.59 (0.32)	p = 0.465	1.64 (0.30)	1.59 (0.32)	p = 0.333
LEMAXL, lb	4.09 (0.42)	4.20 (0.38)	p = 0.003	4.09 (0.43)	4.30 (0.40)	p < 0.001	4.20 (0.39)	4.30 (0.39)	p = 0.002
LEMXKG, lb/kg	1.73 (0.42)	1.82 (0.40)	p = 0.084	1.74 (0.42)	1.95 (0.40)	p = 0.002	1.84 (0.40)	1.95 (0.40)	p = 0.033

*These *t* tests were done using the pair-wise option for missing data; thus, only subjects with data at both points were included in the individual comparisons. The pair-wise procedure created different sample sizes and different means for the variables used in each comparison. The *t* tests were done using the transformed data. SDs are presented in parentheses. See Table 1 for definition of abbreviations.

Table 5—*Comparison of Within-Condition Means Across Time for the Strength Group**

Variables	Time 1 vs Time 2 (n = 30)			Time 1 vs Time 3 (n = 28)			Time 2 vs Time 3 (n = 28)		
PWCL, W	4.57 (0.44))	4.56 (0.47)	p = 0.772	4.56 (0.41)	4.64 (0.35)	p = 0.032	4.64 (0.42)	4.64 (0.35)	p = 0.048
PWCPCS	8,607.9 (2,912.6)	7,580.13 (3,170.2)	p = 0.012	8,597.86 (3,015.6)	8,172.57 (3,978.7)	p = 0.482	7,557.79 (3,171.7)	8,172.57 (3,978.7)	p = 0.325
TOTSC	5.07 (0.40)	5.02 (0.58)	p = 0.669	5.07 (0.42)	5.14 (0.49)	p = 0.440	5.06 (0.58)	5.14 (0.49)	p = 0.478
$\dot{V}O_2$PKG, mL/min/kg	32.54 (5.88)	30.38 (6.21)	p = 0.007 (n = 29)	32.64 (6.22)	30.91 (6.73)	p = 0.065	30.04 (6.20)	30.64 (6.70)	p = 0.485 (n = 27)
FEV_1PT	90.3 (17.85)	86.07 (17.16)	p = 0.052	91.18 (18.07)	90.29 (15.82)	p = 0.646	86.04 (17.72)	90.29 (15.82)	p = 0.048
BCMAXL, lb	3.39 (0.44)	3.52 (0.37)	p = 0.001	3.40 (0.37)	3.62 (0.35)	p < 0.001 (n = 27)	3.53 (0.34)	3.62 (0.35)	p = 0.001 (n = 27)
BCMXKS, lb/kg	0.678 (0.28)	0.769 (0.28)	p = 0.052	0.691 (0.26)	0.847 (0.30)	p = 0.004 (n = 27)	0.766 (0.26)	0.847 (0.30)	p = 0.027 (n = 27)
BPMAXL, lb	4.07 (0.40)	4.21 (0.36)	p < 0.001	4.08 (0.33)	4.26 (0.33)	p < 0.001	4.20 (0.34)	4.26 (0.33)	p = 0.035
BPMXKG, lb/kg	1.61 (0.39)	1.71 (0.39)	p = 0.066	1.62 (0.38)	1.72 (0.40)	p = 0.058	1.70 (0.40)	1.72 (0.40)	p = 0.693
LEMAXL, lb	4.05 (0.56)	4.24 (0.51)	p < 0.001	4.06 (0.49)	4.32 (0.39)	p < 0.001	4.24 (0.47)	4.32 (0.39)	p = 0.009
LEMXKG, lb/kg	1.60 (0.49)	1.78 (0.49)	p = 0.001	1.61 (0.46)	1.83 (0.44)	p < 0.001	1.79 (0.49)	1.83 (0.44)	p = 0.359

*These *t* tests were done using the pair-wise option for missing data; thus, only subjects with data at both points were included in the individual comparisons. The pair-wise procedure created different sample sizes and different means for the variables used in each comparison. The *t* tests were done using the transformed data. SDs are provided in parentheses. See Table 1 for definition of abbreviations.

Aerobic Fitness and Pulmonary Function Measures

The *a priori* hypotheses for aerobic training were that greater changes in fitness and pulmonary function would be obtained in the aerobic group relative to the strength-training group, and that fitness would increase within the aerobic-training group. The GEE was performed on the measure for aerobic fitness (maximum ventilatory oxygen capacity [$\dot{V}O_2$peak]), percentage of predicted FEV_1, and two measures for exercise tolerance, PWC and percentage of predicted PWC. None of these variables produced a significant group-by-time effect. $\dot{V}O_2$ peak and PWC showed significant changes over time (Table 3).

$\dot{V}O_2$peak: $\dot{V}O_2$peak decreased during the first 6 months, and then increased slightly from 6 months to 12 months in the aerobic condition. The same pattern was also found for the strength group. Paired *t* tests were conducted to compare the within-group means at each time point. The strength group showed a significant decrease during the first 6 months, and a significant decrease between baseline and 12 months. The results for the aerobic group show no significant differences for any of the comparisons. Thus, the aerobic group sustained $\dot{V}O_2$peak (Table 4), while the strength group decreased significantly over time (Table 5).

PWC: The increase in PWC from 6 months to 12 months and from baseline to 12 months reached significance for the strength group (Table 5). The aerobic group showed a significant increase from baseline to 12 months (Table 4). Thus, work capacity increased for both conditions, with no difference observed between groups.

Percentage of Predicted PWC: PWC expressed as percentage showed different changes over time for each group based on *t* tests performed on the transformed variable. The mean value for the aerobic group increased during the first 6 months, then decreased slightly from 6 months to 12 months, but the differences did not reach significance (Table 4). The mean for the strength group decreased during the first 6 months, and this decrease was significant. However, mean strength increased from 6 months to 12 months, but this change did not reach significance (Table 5). Thus, no sustained change was seen for percentage of predicted PWC.

FEV_1 Percentage of Predicted: Both groups showed the same pattern of change for FEV_1 percentage of predicted (Tables 4, 5). There was a decrease in the means during the first 6 months, followed by an increase from 6 to 12 months, but these changes did not reach significance for the aerobic group. The results of the paired *t* tests for the strength group show a significant decrease during the first 6 months, followed by a significant increase from 6 to 12 months. There were no significant changes from baseline to 12 months in either group (Tables 4, 5).

Covariate Adjustments: None of the group-by-time analyses for aerobic fitness or pulmonary function measures became significant after adjusting for age or sex. The significant time effect observed for $\dot{V}O_2$peak and the significant time effect observed for PWC in the first GEE algorithms remained significant after adjusting for age and gender.

Height and Weight: Both groups experienced a significant increase in height and weight over time. The mean height of the participants in the strength group increased from 145.17 cm at baseline to 150.15 cm at 12 months ($p < 0.001$). The mean height of the participants in the aerobic group increased from 143.03 cm at baseline to 147.65 cm at 12 months ($p < 0.001$). The mean weight of the participants in the strength group increased from 39.77 kg at baseline to 44.34 kg at 12 months ($p < 0.001$). The mean weight of the participants in the aerobic group increased from 36.18 kg to 39.78 kg during the 12 months of the trial ($p < 0.001$).

QWB Scale: The group-by-time analysis for the total QWB scale did not reach significance (Table 3). Similarly, none of the within-group changes reached significance (Tables 4, 5).

Discussion

This study was designed to test the differential effects of strength vs aerobic training implemented in the each child's residence, as a prerequisite for trials that might confirm health benefits. Youth completed objective measures of strength, aerobic fitness, and pulmonary function. Data were collected by staff, independent of clinical personnel, and were analyzed by investigators separate from clinical personnel. Sixty-seven youth/families volunteered and were assigned to conditions at random. After excluding data for siblings, 62 youth started the trial and 53 youth (85%) by the end of the trial were available for analyses. Considering the illness and the requirements for participation, this is a remarkable completion rate. Examination of the balance between groups showed no significant differences, supporting the success of the random assignment. Finally, analyses were conducted following intent-to-treat rules. Thus, this trial is one of the more rigorous controlled studies of CF exercise.

Not surprising, all strength measures increased over time for the strength group. However, for bench press measures, this relationship did not remain significant after adjustment for body weight. These findings were consistent with our hypotheses about change over time.

The biceps curls was the only strength measure for which a significantly greater increase was obtained for the strength group relative to the aerobic group. This group-by-time difference remained significant after adjustment for age and sex. However, this relationship was not sustained after adjustment for body weight or for increase in height. Thus, this possible training effect cannot be attributed to training independent of growth in weight or height. This finding suggests that strength training might increase biceps strength more than aerobic training. Since strength training could increase body weight, adjustment for body weight might reduce the true effects of training. To better understand strength training effects, comparison with patients who do not obtain physical training is needed.

When the aerobic training outcomes were considered, no group-by-time analyses reached significance, and none became significant after controlling for age or sex. Thus, aerobic training did not produce greater fitness or greater pulmonary function than strength training.

The aerobic training group also did not show increases in aerobic fitness measures over time. However, the aerobic training group showed increases in PWC, but this was not sustained when computed as a percentage of predicted. Thus, surprisingly, the aerobic training condition did not result in aerobic training effects. Use of the step machine was expected to increase leg strength in the aerobic group, and this was confirmed for both maximum leg strength and strength adjusted for body weight.

Surprisingly, the strength group also showed an increase in leg strength with and without adjustment for body weight, even though the strength training equipment/instruction did not include leg exercises. These results suggest generalization took place, possibly increased use of other muscle groups. Future studies should include measures of leg exercises and activity that increase leg strength to explore possible mechanisms.

The aerobic training group produced the most surprising results for upper-body strength measures. Significant increases in biceps and bench press strength were observed. These increases were apparent after adjustment for body weight, but did not remain significant. It is possible that the increase in arm strength was a side effect of the step machine in relation to the size of the children. It is possible that they used their arms to balance and to initiate stepping. This could have inadvertently trained upper-body strength.

An increase in strength was associated with both training procedures. In absence of a no-training control condition, it is not possible to attribute these changes to the interventions with confidence. However, it is plausible that both training conditions contributed to increased strength. This association justifies follow-up analyses with designs that include "usual medical care" control conditions. It also appears that both training procedures result in some generalization to outcomes usually attributed to the opposite type of training. When this study was proposed, the IRBs precluded the use of a no-exercise usual medical care control. However, these results demonstrate the importance of including both specific types of exercise and usual-care control conditions. The failure to obtain clear training effects from either type of training provides evidence suggesting that comparing interventions to usual medical care will not increase risk to patients in the experimental condition, and will not deprive patients in usual medical care with known beneficial physical training. This later point might persuade IRB review committees to allow usual-care control conditions. Future trials should be designed to include sufficient numbers of youth to compare training to usual-medical-care control conditions.

Both training procedures were associated with significant increases in body weight. Since body weight is one of the more important predictors of morbidity/mortality among children with CF, this is a promising outcome that might be due to both types of physical activity training. Both types of training were also associated with increased height. This is most likely due to age, since all youth were as much as 1 year older by follow-up measures. It is also possible, however, that both types of training contributed to overall growth. Thus, our use of weight and height as a covariate represents conservative tests of the *a priori* hypotheses. Given the predictive association between weight/height and survival time for children with CF, future studies should be designed with greater statistical power. This should include a more intensive intervention, especially for aerobic training, a comparison with usual-care controls (from which greater intervention vs control differences can be expected) and a larger sample size from which small effects may remain significant even after control for possible confounding variables.

We chose the stair-stepping exercise machine over a treadmill for financial considerations, and over a stationary cycle to avoid training one group on the same equipment that all subjects used for outcome measures. In retrospect, this might have been a mistake. While use of two different types of machines reduced error attributable to learning the test, it may have increased error due to physical and psychological difficulties performing the exercise. Small-for-age children had more difficulty than expected using the stepping machines. This may have caused them to be less reliable in practicing the recommended exercises, and it may have made it more difficult to exert the same effort for sufficient time. While we do not have explicit measures of adherence to the recommended exercise practice, the limited aerobic effects and the somewhat larger rate of dropout in the aerobic condition suggests possible problems with adherence. Future studies should use aerobic training procedures well matched to the size of the child, and include measures of adherence to the recommended exercise regimen. Boas et al[49] indicated that parents of children with CF perceive a significantly greater number of barriers to their child's participation in exercise as compared to parents with healthy children. Future studies will need to address these barriers.

Overall, we conclude that strength training may increase upper-body strength for children with CF. We also tentatively conclude that both strength and aerobic training, at least when based on stepping machines, may increase strength in the upper and lower body. We also conclude that both types of training may increase body weight. These conclusions should be confirmed by additional controlled trials that include usual-care control conditions. Finally, future trials of combination training are needed in order to determine possible health benefits to patients with CF from either or both exercise regimens.

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